RADIESSE
INJECTABLE IMPLANT
INSTRUCTIONS FOR USE

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed physician, or properly licensed practitioner.

DESCRIPTION

Radiesse is a sterile, latex-free, non-pyrogenic, semi-solid, cohesive subdermal implant. The principle durable component of Radiesse is synthetic calcium hydroxylapatite, a biomaterial with over twenty years of use in orthopedics, neurosurgery, dentistry, otolaryngology and ophthalmology. Calcium hydroxylapatite is the primary mineral constituent of bone and teeth. The semi-solid nature of Radiesse is created by suspending calcium hydroxylapatite in a gel carrier that consists primarily of water (sterile water for injection USP) and glycerin (USP). The gel structure is formed by the addition of a small amount of sodium carboxymethylcellulose (USP). The gel is dissipated *in vivo* and replaced with collagen and other soft tissue ingrowth, while the calcium hydroxylapatite remains at the site of injection to form a scaffold for the new tissue formation. The result is intended to be long-term soft tissue augmentation. Radiesse (0.3 cc and 1.3 cc) has a particle size range of 25-45 microns and should be injected with a 25 to 27 gauge needle.

INTENDED USE / INDICATIONS

Radiesse is indicated for the correction of facial lipoatrophy (facial fat loss).

CONTRAINDICATIONS

- Radiesse is not to be used in patients with known hypersensitivity to any of the components.

WARNINGS

- Use of Radiesse in any person with active skin inflammation or infection in or near the treatment area should be deferred until the inflammatory or infectious process has been controlled.
- Injection procedure reactions to Radiesse have been observed consisting mainly of short-term bruising, redness and swelling. Refer to adverse events section for details.
- Special care should be taken to avoid injection into the blood vessels. An introduction into the vasculature may occlude the vessels and could cause infarction or embolism.

PRECAUTIONS

- The calcium hydroxylapatite (CaHA) particles of Radiesse have been shown to be radiopaque. Studies have shown that the CaHA particles are clearly visible on CT Scans and may be visible in standard, plain radiography. The study did not provide any evidence of significant risk of the injected Radiesse potentially masking abnormal tissues or being interpreted as tumors in CT Scans. Patients need to be informed of the radiopaque nature of Radiesse, so that they can inform their primary care health professionals as well as radiologists.
- Radiesse is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged. Do not use if the syringe end cap or syringe plunger is not in place.
- As with all transcutaneous procedures, Radiesse injection carries a risk of infection. Standard precautions associated with injectable materials should be followed. No infections have been reported in the clinical study. Refer to adverse events section for details.
- Safety of Radiesse for use during pregnancy, in breastfeeding females or in patients under 18 years has not been established.

- Patients who are using medications that can prolong bleeding, such as aspirin or warfarin, may, as with any injection, experience increased bruising or bleeding at the injection site.
- Universal precautions must be observed when there is a potential for contact with patient body fluids. The injection session must be conducted with aseptic technique.
- After use, treatment syringes and needles may be potential biohazards. Handle accordingly and dispose of in accordance with accepted medical practice and applicable local, state and federal requirements.
- The patient should be informed that he or she should minimize exposure of the treated area to extensive sun or heat exposure for approximately 24 hours after treatment.

ADVERSE EVENTS

In a prospective, open label study of 100 patients at three U.S. sites, adverse events reported after Radiesse treatments are provided in Table 1.

Table 1
Maximal Severity and Duration of Local Adverse Events at Any Time

Adverse Event	Number of Patients With Event	95% Confidence Interval	Maximal Severity			Duration[1] (Days)
			Mild	Moderate	Severe	
Allergic Reaction	0	(0.0%– 0.0%)	0 0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Echymosis	65	(54.8% - 74.2%)	34 (52.3%)	26 (40.0%)	5 (7.7%)	7.7, 4.8 (1.0 -27.0)
Edema	99	(94.6% - 100.0%)	46 (46.5%)	49 (49.5%)	4 (4.0%)	5.0, 5.4 (1.0 - 63.0)
Embolization	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Erosion	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Erythema	57	(46.7% - 66.9%)	34 (56.7%)	23 (40.4%)	0 (0.0%)	4.4, 3.0 (1.0 – 22.0)
Extrusion	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Granuloma	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Hematoma	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Infection	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Necrosis	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Needle Jam	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Nodule	0	(0.0%– 0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0, 0 (0.0-0.0)
Pain	39	(29.4% - 49.3%)	25 (64.1%)	13 (33.3%)	1 (2.6%)	5.2, 4.5 (1.0 – 26.0)
Pruritis	21	(13.5% - 30.3%)	18 (85.7%)	3 (14.3%)	0 (0.0%)	6.9, 6.9 (1.0 – 26.0)
Other	58	(47.7% - 67.8%)	40 (69.0%)	17 (29.3%)	1 (1.7%)	31.3, 49.8 (1.0 – 208.0)
Total	339		197 (58.1%)	131 (38.6%)	11 (3.2%)	

CLINCAL STUDIES

The safety and effectiveness of Radiesse for the treatment of lipoatrophy was evaluated in a prospective, open-label, multi-center study of 100 patients.

Study Design

The study was designed to assess the safety and effectiveness of Radiesse for the treatment of facial lipoatrophy with one hundred (100) patients receiving treatment. Patients received an initial treatment (initial injection and an additional injection at 1 month as needed). Six months later, all patients were assessed for the need for a touch up injection. Effectiveness was assessed at 3, 6 and 12 months from initial treatment by means of a Global Aesthetic Improvement Scale (GAIS) rating, cheek skin thickness

1 Mean, Standard Deviation, Minimum and Maximum

measurements, and patient satisfaction assessment. Safety was assessed by the recording of adverse events through 12 months.

Endpoints

Primary:

The primary endpoint of the study was to evaluate the correction of lipoatrophy 3 months after treatment by comparing changes from baseline on the GAIS. The GAIS is a 5-category scale (Very much improved, much improved, improved, no change and worse).

Secondary:

The secondary endpoints of the study were to evaluate the correction of facial lipoatrophy 6 months after treatment by comparing changes from baseline on the GAIS and 3 and 6 months after treatment by comparing changes from baseline in cheek skin thickness measurements.

Results

Patient Demography / Injection Information:

The study enrolled a population of predominantly multi-ethic, non-smoking males (percentage male) with a mean age of 48 years. Forty-four (44) percent of patients were Black, Hispanic or Asian. Fifty-six (56) percent were Caucasian. Fifty-one (51) percent of patients had a Fitzpatrick Skin score of ≥IV. All injections were performed with a 25G, 1½ inch needle. Mean initial treatment volumes were 4.8cc for the initial injection and 1.8cc at 1 month if necessary (85% of patients were injected at 1 month). At 6 months, the mean touch up volume was 2.4cc (91% of patients). Four (4) percent of patients received only one injection, 18% of patients received a total of two injections and 78% of patients received a total of three injections. No patient received more than three injections.

Effectiveness:

A live GAIS rating was determined at 3, 6 and 12 months (see Table 2).

Table 2
GAIS Ratings

% of Patients	3 Month (Primary Endpoint) N = 100	6 Month N = 98	12 Month N = 98
Very Much Improved	26%	7%	31%
Much Improved	72%	86%	53%
Improved	2%	7%	16%
No Change	0%	0%	0%
Worse	0%	0%	0%
TOTAL Improved	**100%**	**100%**	**100%**

Patients received skin thickness measurement of their left and right cheeks at baseline, 3, 6 and 12 months (see Table 3).

Table 3
Cheek Skin Thickness Measurements

	BASELINE	3 MONTH			6 MONTH			12 MONTH		
	Mean (N=100)	Mean (N=100)	Δ From Baseline	P-Value	Mean (N=97)	Δ From Baseline	P-value	Mean (N=98)	Δ From Baseline	p Value
Left Cheek	4.7mm	7.3mm	2.6mm	<.0001	7.1mm	2.4mm	<.0001	6.9mm	2.2mm	<0.0001
Right Cheek	4.9mm	8.0mm	2.1mm	<.0001	7.5mm	2.7mm	<.0001	7.3mm	2.5mm	<0.0001

Patients provided responses to a 5-question patient satisfaction questionnaire at 3, 6 and 12 months (see Table 4).

Table 4
Patient Satisfaction Assessment

	3 Months N = 100	6 Months N = 98	12 Months N = 98
	Yes	Yes	Yes
Would you recommend Radiesse treatment?	99%	99%	99%
Has the Radiesse treatment been beneficial to you?	100%	100%	100%
Do you feel more attractive since receiving Radiesse treatment?	98%	98%	99%
Is your emotional wellbeing better since receiving Radiesse?	91%	96%	97%
Do you have more confidence in your appearance since receiving Radiesse?	98%	98%	99%

Conclusions

Radiesse is safe and effective for the treatment of lipoatrophy with improvement lasting 12 months from treatment with generally mild and transient inject-site side effects and no nodules or granulomas.

INDIVIDUALIZATION OF TREATMENT

Before treatment, the patient's suitability for the treatment and the patient's need for pain relief should be assessed. The outcome of treatment with Radiesse will vary between patients. In some instances, additional treatments may be necessary depending on the size of the defect and the needs of the patient.

DIRECTIONS FOR USE

GENERAL

The following is required for the percutaneous injection procedure:

- Radiesse syringe(s)
- 25-27 gauge needle with Luer lock fittings

1. Prepare patient for percutaneous injection using standard methods. The treatment injection site should be marked and prepared with a suitable antiseptic. Local or topical anesthesia at the injection site should be used at the discretion of the physician.
2. Prepare the syringes of Radiesse and the injection needle(s) before the percutaneous injection. A new injection needle may be used for each syringe, or the same injection needle may be connected to each new syringe.
3. Remove foil pouch from the carton. Open the foil pouch by tearing at the notch, and remove the syringe from the foil pouch. *There is a small amount of moisture normally present inside the foil pouch for sterilization purposes; this is not an indication of a defective product.*

4. Remove the Luer syringe cap from the distal end of the syringe prior to attaching the needle. The syringe of Radiesse can then be twisted onto the Luer lock fitting of the needle. **The needle must be tightened securely to the syringe and primed with Radiesse.** If excess Radiesse is on the surface of the Luer lock fittings, it will need to be wiped clean with sterile gauze. Slowly push the syringe plunger until Radiesse extrudes from the end of the needle. If leakage is noted at the Luer fitting, it may be necessary to tighten the needle, or to remove the needle and clean the surfaces of the Luer fitting or, in extreme cases, replace both the syringe and the needle.
5. Locate the initial site for the implant. Scar tissue and cartilage may be difficult or impossible to treat. Avoid, if possible, passing through these tissue types when advancing the injection needle.
6. The amount injected will vary depending on the site and extent of the restoration or augmentation desired. Radiesse should be injected subdermally.
7. Use a 1:1 correction factor. No overcorrection is needed.
8. If significant resistance is encountered when pushing the plunger, the injection needle may be moved slightly to allow easier placement of the material or it may be necessary to change the injection needle. No needle jams occurred in the clinical study, but such jams are possible with needles smaller than 27g or if the needle is not properly tightened onto the syringe.
9. Advance the needle into the subdermis to the starting location. Carefully push the plunger of the Radiesse syringe to start the injection and slowly inject the Radiesse material in linear threads while withdrawing the needle. Continue placing additional lines of material until the desired level of correction is achieved.
10. Insert needle with bevel down at approximately a 30° angle to the skin. Needle should slide under the dermis to the point you wish to begin the injection. This should be easily palpable with the non-dominant hand.
11. Apply slow continuous even pressure to the syringe plunger to inject the implant as you withdraw the needle. The implant material should be completely surrounded by soft tissue without leaving globular deposits. The injected area may be massaged as needed to achieve even distribution of the implant material.

PATIENT COUNSELING INFORMATION

Refer to Radiesse Patient Information Guide.

STORAGE

Radiesse should be stored at a controlled room temperature between 15° C and 32° C (59° F and 90° F). The expiration date, when stored in these temperatures, is two years from date of manufacture. Do not use if the expiration date has been exceeded.

DISPOSAL

Used and partially used syringes and injection needles could be biohazardous and should be handled and disposed of in accordance with facility medical practices and local, state or federal regulations.

WARRANTY

BioForm Medical Inc. warrants that reasonable care has been exercised in the design and manufacture of this product.

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